Factors in Choosing Egg or Cell-Based Technologies For Influenza Vaccines

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IFPMA
Influenza Vaccine Supply
International Task Force

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About the IFPMA Influenza Vaccine Supply international task force

Established in 2002 to bring together research-based vaccine manufacturers from around the world, which are conducting R&D to develop and produce safe, effective, high-quality human vaccines against seasonal, avian and pandemic influenza.

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Egg-Based Influenza Vaccine Types

The currently available seasonal influenza vaccines are almost exclusively prepared using the **egg-based culture** technique with the following virus types:

1. Whole virus vaccines consisting of inactivated viruses
2. Split virus vaccines consisting of inactivated virus particles disrupted by detergent treatment
3. Subunit or surface antigen vaccines consisting essentially of purified hemagglutinin and neuraminidase, from which other virus components have been removed
4. Live attenuated (cold-adapted) virus vaccines consisting of weakened (non-pathogenic) whole virus

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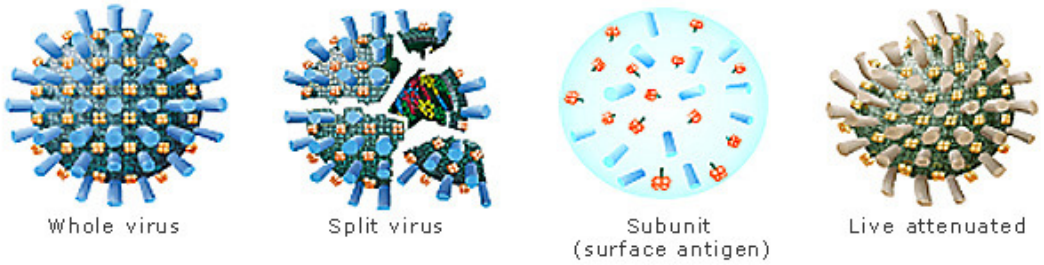
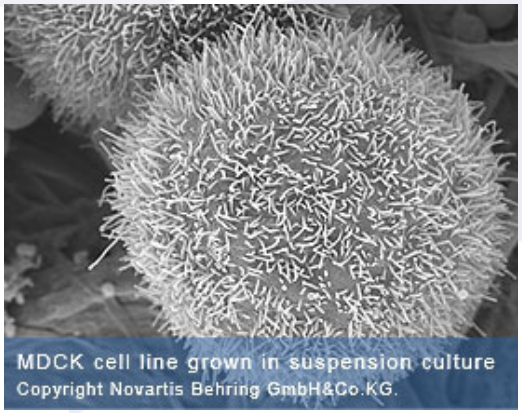
Cell-Based Influenza Vaccine Types





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Cell-Based Influenza Vaccines: Current Status

1. Seasonal Vaccines: ≈ 3* licensed vaccines in the last 3 years
2. Current commercial scale bulk production in EU
3. One product marketed in 2007 in EU; one in Russia
4. Clinical Trials (Phase I-III) ongoing
5. Pandemic Vaccines: ≈ 3* products licensed for A/H1N1
6. Several H5N1 Flu Cell Culture Clinical Trials ongoing

* Based on members feedback

Advantages & Challenges: Egg-Based Influenza Vaccines

Advantages	Challenges
Safe use – more than 60 years of production	Open system, potential microbial contamination from eggs
Successful scale up to 300,000 eggs per day	Equipment specific to influenza production, dedicated facility
Availability of egg-based high yield viruses (reassortants)	Egg-adaptation might change antigen immunogenicity with respect to circulating strains
Known regulatory path	Intensive purification process for inactivated vaccines (ultracentrifugation)

Advantages & Challenges: Cell-Based Influenza Vaccines

Advantages	Challenges
Accurate process control, closed system, thus improved aseptic operations	Relatively new technology for influenza vaccine with relatively new regulatory path
Elimination of egg components in the vaccine (suitable for allergies)	Requirement for more sophisticated equipment in cell culture processes. Cost disadvantages, not only in capital investment
Independence from eggs, avoid risk of avian retrovirus	Maintenance of qualified cell culture line, cell qualification requirements
Cell lines and equipment might potentially be used for a variety of vaccine products	Complex adventitious agents testing
	Intensive purification process for inactivated vaccines (ultracentrifugation)

Additional Considerations

1. Cell Culture Technology implementation may be easier if cell culture manufacturing / infrastructure is already present
2. Technology Transfer for biologicals presents a high degree of technical difficulty
3. Quality control, training and compliance with regulations are by far the greatest tasks in manufacturing vaccines and require constant management

Conclusions

1. Egg and cell-based influenza vaccine production offer distinct advantages and challenges
2. Egg-based technology has proven safe and effective for more than 60 years
3. Cell Culture Technology has been used for seasonal and pandemic influenza vaccine production and might potentially be applied to a variety of vaccines
4. Key additional considerations for choice of technology include presence of infrastructure plus tech transfer , quality and regulatory requirements.

BACKUP SLIDES

Influenza Vaccine Manufacturing: How Different Types of Vaccines Are Made

1. To produce the **split virus** and **subunit** vaccines, the whole virus is subjected to disruption with a surfactant, which solubilizes the viral membrane.
2. For **subunit** vaccines, the internal subviral core of the virus is separated from the surface proteins on the basis of their differing sedimentation rates.
3. With **split** virus vaccines, the choice and use of surfactant ensures that the subviral core itself is disassembled.
4. For the US market, **live virus** vaccines are formulated to contain 106.5-7.5 median tissue culture infectious doses of live attenuated influenza virus. Live virus vaccines are also manufactured for use in other countries.
5. All vaccines require purification, at least one buffer exchange step, formulation, fill and finish.
6. Cold chain storage and distribution are also required.